Sexual transmission of HIV-1 among injection drug users in San Francisco, USA: risk-factor analysis

Alex H Kral, Ricky N Bluthenthal, Jennifer Lorvick, Lauren Gee, Peter Bacchetti, Brian R Edlin

Summary

Background Many new HIV-1 infections in the USA occur in injection drug users (IDUs). HIV-1 seroconversion of IDUs is mainly associated with injection-related risk factors. Harm-reduction programmes concentrate on injection-risk behaviour. We aimed to establish whether injection or sexual risk factors, or both, were associated with HIV-1 antibody seroconversion of street-recruited IDUs in San Francisco, from 1986 to 1998.

Methods IDUs were enrolled every 6 months from four community sites. We did a nested case-control study comparing 58 respondents who seroconverted between visits with 1134 controls who remained seronegative. Controls were matched with cases by sex and date. Adjusted odds ratios and 95% CI were calculated for men and women by use of conditional logistic regression.

Findings Men who had sex with men were 8·8 times as likely to seroconvert (95% CI 3·7–20·5) as heterosexual men. Women who reported having traded sex for money in the past year were 5·1 times as likely as others to seroconvert (95% CI 1·9–13·7). Women younger than 40 years were more likely to seroconvert than those 40 years or older (2·8 [1·05–7·6]), and women who reported having a steady sex-partner who injected drugs were less likely to seroconvert than other women (0·32 [0·11–0·92]).

Interpretation HIV-1 seroconversion of street-recruited IDUs in San Francisco is strongly associated with sexual behaviour. HIV-1 risk might be reduced by incorporation of innovative sexual-risk-reduction strategies into harm-reduction programmes.

Lancet 2001; **357:** 1397–401

Urban Health Study, Institute for Health Policy Studies and Departments of Family and Community Medicine (A H Kral PhD, J Lorvick BA, L Gee MPH, B R Edlin MD)**, and Epidemiology and Biostatistics** (P Bacchetti PhD)**, University of California, San Francisco; Division of Public Health Biology and Epidemiology, School of Public Health, University of California, Berkeley,** (A H Kral)**; and Health Program and Drug Policy Research Center, RAND and Department of Psychiatry, Charles R Drew University of Medicine and Science, Los Angeles, CA, USA** (R N Bluthenthal PhD)

Correspondence to: Dr Alex H Kral, Urban Health Study, UCSF, 3180 18th Street, San Francisco CA 94110, USA (e-mail: alkral@itsa.ucsf.edu)

Introduction

A large proportion of new HIV-1 cases in the USA are injecting drug users (IDUs).[1] HIV-1 seroconversion of IDUs is mainly associated with injection-related risk factors.[2–6] However, few seroconversion studies have been done since 1992 and in only two was an association seen between sexual risk factors and seroconversion.[5,6] Researchers commonly concentrate on injection-related risk factors and ignore sexual risk.[7]

In comparison with other US cities, HIV-1 prevalence among IDUs in San Francisco is moderate[8] and has been stable at 10–14% since 1987.[9,10] HIV-1 prevalence among men who have sex with men in this city is high (30%).[11] In San Francisco, HIV-1 incidence among IDUs in methadone clinics in the late 1980s was 1·9%,[5] which was similar to an estimate for 15 other US cities at that time,[4] and to another for 17 US cities in the mid-1990s (1·5%).[12] Estimates of HIV-1 incidence in San Francisco for men who have sex with men are also similar to those of IDUs (1·2–2·8%).[13,14]

San Francisco has adopted a harm-reduction philosophy[15] for prevention of HIV-1 in IDUs, which started with community-health outreach programmes in 1985, so-called bleach and teach programmes in 1986, a syringe-exchange programme in 1988, and a policy of drug treatment on demand in 1997. Harm-reduction programmes are controversial in the USA, because workers help drug users to reduce risks whether they intend to enter drug treatment or not. These programmes have reduced injection-related risks even in regions where they are illegal.[16] Few harm-reduction programmes in San Francisco have attempted to reduce sexual risk.

We assessed data from the Urban Health Study to establish risk factors for HIV-1 seroconversion among street-recruited IDUs.

Methods

Recruitment

Active IDUs were recruited for the Urban Health Study in three inner-city communities in San Francisco from 1986, and in a fourth from 1996. 6-monthly surveys included 170–250 IDUs in each community. We assessed data from 23 surveys done from 1986 to 1998. Respondents were recruited in natural settings with targeted sampling methods.[17] Communities selected had high concentrations of IDUs according to drug-treatment admission data, police arrest data, direct observation, and earlier ethnographic studies. Respondents were not recruited from institutional locations such as drug-treatment programmes, homeless shelters, correctional facilities, clinics, or hospitals. The eligibility criterion was recent intravenous drug use (past 30 days). New respondents were screened for visible signs of recent subcutaneous or intravenous drug use (so-called tracks, or recently punctured veins). Respondents were permitted to participate in subsequent surveys irrespective of whether they had continued to inject drugs. Repeat respondents were identified by checking information against that held in a database on a lap-top computer. Every 6 months, a new sample was recruited; previous participants were not helped to return to the study. This method

allowed us to assess new cases of HIV-1 infection from repeat visits of participants.[5]

Procedures

Eligible respondents had a private interview and counselling session with a trained interviewer and counsellor. All participants gave informed consent before a structured questionnaire was given by the interviewer. Questionnaires included: demographic factors (ethnic origin, age, eduction, homelessness, and neighbourhood); drug use (sharing syringes and drug cookers, injection frequency, number of years of injecting, injection drug of choice, crack-cocaine use, alcohol use, and sources of syringes); sexual practices (number of sex partners, number of male sex-partners, men who have sex with men, sex for money, safe sex [no sex or condom use at all times during vaginal or anal sex], steady sex-partner, steady sex-partner who injected drugs, and self-reported sexually transmitted diseases, including gonorrhoea, chlamydia, syphilis, and genital herpes); and use of services (syringe-exchange use, including usual source of needles, substance-abuse treatment, contact with outreach workers, number of previous HIV-1-test results, and number of previous Urban Health Study visits).

Most questions referred to the previous year, although some were about the past 6 months (safe syringe source), past month (sharing syringes, sharing drug cookers, injection frequency, and syringe-exchange use), or current behaviour (steady sex-partner, steady sex-partner who injected drugs, homelessness, and substance-abuse treatment). 20 participants who were interviewed during 1986–88 were not asked about sex work in the past year; they were classed as having done sex work in the past year if they reported sex work in the past 5 years and more than two male sex-partners in the past year.

After interview, respondents were advised about their risk behaviours, given HIV-1 pretest counselling, and referred to medical and social services as needed. Phlebotomists took blood for HIV-1-antibody testing. Participants were paid US$15 and asked to return for HIV-1-test results and counselling 4 weeks (1986–94) or 2 weeks (1995–98) after interview. Methods were approved by the Committee on Human Subjects Research at University of California, San Francisco.

Blood samples were analysed for HIV-1 antibodies by ELISA. Positive specimens were further tested by western blot, and were confirmed as positive if results showed reactive bands at two of the following locations: p24 or gp41; and gp120 or gp160.[18]

Cases were participants who seroconverted, controls were those who did not. Controls were matched to cases of the same sex. All controls who were tested in the same surveys in which a seroconverter had their last negative and first positive test results (but were not tested in between those times) were matched to that case. Each control was matched to one case, with an algorithm that selected the least common of all possible observation windows for each control.

Statistical analysis

Participants were not required to give their names, hence a retrospective and systematic approach was used to link more than one observation of the same individual. First, a list of possible links was generated from identifying information: date of birth, sex, ethnic origin, the first two (1986–93) or four (1993–98) letters of the mother's maiden name, and US state or country of birth. Links were verified by checking names and addresses from a contact-details form (volunteeered by about half of all respondents) or by identifying information from the questionnaires that should remain constant—such as year of tattoos, pregnancies, or jail sentences. Individuals who were HIV-1 positive at baseline were excluded, the remainder were eligible for the case-control study. A crude incidence rate was calculated for eligible participants with person-years of observation as the denominator.

Cases were defined as initially HIV-1-negative participants who then had a positive HIV-1-antibody-test result in our study. We excluded those who had a gap in observation (observation window) of more than 3 years between their last negative HIV-1-antibody-test result and their first positive result, to ensure that risk factors that led to seroconversion were likely to have been ascertained in our interviews.

We compared our case-control sample with all HIV-1-antibody-negative participants by Fisher's exact and Kruskal-Wallis tests. We used behavioural-risk data from the first follow-up interviews after positive HIV-1-antibody-test result, and the corresponding interviews for controls, to assess risk factors for HIV-1 seroconversion. Since cases and controls were matched by observation window and sex, we did regression analysis conditioned on observation window and stratified all analyses by sex. Conditional logistic regression for matched data was done for bivariate and multivariate analyses with Statistical Analysis System software (version 8.00, SAS Institute; Cary, NC, USA). In all analyses, odds ratios and adjusted odds ratios with 95% CI were calculated. All variables associated with seroconversion in bivariate analysis ($p<0·10$) were assessed for inclusion in multivariate analysis. Only significant variables ($p<0·05$) were retained in multivariate models. Interactions between all main effects were taken into account in each model.

Results

We did 13 099 interviews and HIV-1-antibody tests. We identified 6115 different participants, of whom 2120 took part more than once. 1865 individuals were eligible for the case-control study. Mean (SD) number of observations per eligible person was 4·0 (2·8). 70 participants were classed as cases, of whom nine were excluded. The median observation time of the nine excluded seroconverters was 5·5 years (range 3·5–9·0). We excluded two cases for whom controls could not be found and one whose sex we did not know. 58 participants became cases, and 1134 controls. Table 1 shows the observation windows in which seroconversion occurred for cases included in our analysis. Table 2 shows the number of controls per case. The average number of controls per case was 19·6 (median 12, range 1–96).

Seroconverters were distributed evenly throughout the

Years	Cases (n=58)
0·5	22
1·0	14
1·5	7
2·0	8
2·5	4
3·0	3

Table 1: **Number of years between last HIV-negative and first HIV-positive test result**

Number of controls per case	Number of cases represented (n=58)
1	1
2–5	15
6–10	10
11–30	16
31–96	16

Table 2: **Number of controls matched per case**

Risk factor	Men		Women	
	HIV sero-converter (n=31)	Seronegative control (n=775)	HIV sero-converter (n=27)	Seronegative control (n=359)
Ethnic origin				
White	15 (48%)	221 (29%)	12 (44%)	96 (27%)
African American	11 (35%)	435 (54%)	8 (30%)	201 (56%)
Hispanic	3 (10%)	76 (19%)	4 (15%)	36 (10%)
Other	2 (6%)	43 (6%)	3 (11%)	3 (7%)
Age				
Median (IQR) years	37 (35–46)	43 (38–48)	37 (35–41)	41 (36–45)
<40 years	17 (55%)	233 (30%)	19 (70%)	147 (41%)
40–49 years	10 (32%)	383 (49%)	7 (26%)	180 (50%)
≥50 years	4 (13%)	159 (21%)	1 (4%)	32 (9%)
Drug use				
Injected drugs ≤20 years*	20 (71%)	250 (35%)	20 (83%)	175 (52%)
Speedball† injection in past year*	11 (37%)	425 (58%)	17 (63%)	171 (48%)
Heroin injection in past year	19 (61%)	624 (82%)	22 (81%)	286 (80%)
Cocaine injection in past year	15 (48%)	278 (36%)	14 (52%)	100 (28%)
Amphetamine injection in past year	18 (58%)	211 (28%)	9 (33%)	63 (18%)
Smoked crack cocaine in past year*	18 (64%)	428 (61%)	18 (75%)	226 (67%)
Currently in substance-abuse treatment	4 (13%)	124 (16%)	5 (19%)	71 (20%)
Other factors				
Recruited in Tenderloin neighbourhood	21 (68%)	272 (36%)	6 (22%)	82 (23%)
Considers self homeless*	11 (38%)	228 (31%)	9 (33%)	109 (31%)
Men who have had sex with men in past year*	14 (45%)	72 (9%)	NA	NA
Traded sex for money in past year*	3 (10%)	39 (5%)	17 (63%)	83 (24%)
Steady partner who injected drugs	13 (42%)	212 (28%)	6 (23%)	175 (49%)

NA=not applicable. *Values are missing for no more than three cases and 70 controls (men), and three cases and 23 controls (women). †Speedball=heroin with cocaine or amphetamine.

Table 3: **Risk-factors assessed at first follow-up interview after positive HIV-antibody-test result and corresponding control interview**

Risk factor	Odds ratio (95% CI)	
	Men	Women
Demographic factors		
Ethnic origin		
African American	0·34 (0·15–0·77)	0·36 (0·15–0·87)
Hispanic	0·94 (0·27–3·20)	1·20 (0·36–3·90)
Other	1·20 (0·28–5·60)	1·70 (0·44–6·70)
White	1·00	1·00
Recruited in Tenderloin neighbourhood	3·80 (1·70–8·50)	0·84 (0·32–2·20)
Aged <40 years	2·10 (0·96–4·40)	3·00 (1·20–7·40)
Homeless*	1·20 (0·54–2·70)	1·20 (0·47–2·80)
Injection risk factors		
Speedball† injection in past year*	0·38 (0·17–0·83)	2·00 (0·84–4·60)
Heroin injection in past year	0·29 (0·13–0·66)	1·30 (0·45–3·70)
Cocaine injection in past year	1·30 (0·62–2·90)	2·50 (1·12–5·70)
Amphetamine injection in past year	4·30 (2·00–9·60)	2·10 (0·91–5·10)
Smoked crack cocaine in past year*	1·30 (0·55–3·00)	1·90 (0·73–5·20)
Shared syringes in past year*	1·80 (0·79–4·00)	0·75 (0·28–2·00)
Shared drug cookers in past year*	0·75 (0·42–1·40)	0·85 (0·51–1·40)
Number of injections in past month	0·994 (0·985–1·002)	1·000 (0·997–1·003)
Injected drugs ≤20 years*	3·80 (1·60–9·10)	4·50 (1·50–13·90)
Currently in substance abuse treatment	0·92 (0·30–2·80)	0·97 (0·35–2·70)
Syringe exchange usual source of syringes (past 6 months)	1·10 (0·46–2·70)	1·50 (0·50–4·60)
Sexual risk factors		
Men who have had sex with men*‡	8·80 (3·70–20·50)	NA
Traded sex for money in past year*	1·70 (0·45–6·60)	6·30 (2·50–15·80)
Number of sex partners in past 6 months*	1·02 (1·01–1·03)	1·002 (1·000–1·004)
Ever had chlamydia	0§	4·30 (1·70–11·10)
Steady sex-partner injected drugs*	2·10 (1·00–4·40)	0·31 (0·11–0·86)
Unprotected vaginal sex in past year*	3·30 (0·36–30·3)	0·58 (0·12–2·80)

NA=not applicable. *Values are missing for no more than three cases and 70 controls (men), and three cases and 23 controls (women). †Speedball=heroin with cocaine or amphetamines. ‡Includes men who reported sex with men in the past year either at follow-up or baseline interview.§None of the 16 male respondents who reported chlamydia was a seroconverter (p=0·99).

Table 4: **Risk factors for HIV seroconversion in bivariate analysis**

study period. We used the midpoint between last negative HIV-1-antibody test result and first positive result as the date of seroconversion. 19 seroconversions occurred between March, 1986, and June, 1990; 20 between July, 1990, and June, 1994; and 19 between July, 1994, and January, 1998. These results do not imply a steady incidence rate, because different numbers of HIV-1-antibody-negative people were followed up in each period. Six seroconverters reported already knowing that they were HIV-1-antibody positive at the time of their first positive test result in the study.

The crude incidence rate among multiple-visit participants was 1·2% per year (95% CI 1·0–1·5). The case-control analysis included 1192 cases and controls; we excluded 4923 HIV-1-negative IDUs. Some differences between the groups were significant. IDUs in the case-control analysis were older than those excluded (median age 42 *vs* 38 years, p<0·0001), and were more likely to be African American than of other ethnic origin (655/1179 [56%] *vs* 1990/4876 [41%], p<0·0001), and to have a longer injection history (median duration 22 *vs* 19 years, p<0·0001).

Case-control IDUs were also less likely than those excluded to: be homeless (357/1142 [31%] *vs* 1703/4123 [41%], p<0·0001); have injected cocaine in the past year (408/1078 [38%] *vs* 2164/4683 [46%], p=0·035); have injected speedball (heroin plus cocaine or amphetamines) in the past year (624/1107 [56%] *vs* 2430/4035 [60%], p=0·021); have shared syringes in the past 30 days (279/1156 [24%] *vs* 2034/4848 [42%], p<0·0001); and be in drug treatment (204/973 [21%] *vs* 1122/4293 [26%], p=0·001). Sex, sexual preference, sex work, heroin injection in the past year, and amphetamine injection in the past year did not differ significantly between groups.

Nearly half the case-control sample were African American, more than half were 40 years or older, and a third were homeless (table 3). Most used more than one substance (heroin, cocaine, or crack cocaine) and fewer than a fifth were in substance-abuse treatment at follow-up interview.

Several variables were significantly associated (p<0·05) with seroconversion in bivariate analysis: demographic factors (race, neighbourhood, and age), sexual risk factors (men who have sex with men, sex work, number of sex partners, having a steady sex-partner who injected drugs, and self-report of chlamydia), drug preference, and duration of injection behaviour (table 4). The only factors significantly associated with HIV-1 seroconversion in both men and women were: being African American, shorter duration of injection behaviour, and number of sex partners. For men, having a steady sex-partner who injected drugs increased the likelihood of seroconversion, whereas for women the likelihood was decreased. For men and women, having no steady sex-partner and having a steady

Independent factor	Adjusted odds ratio (95% CI)
Women*	
Traded sex for money in past year	5·10 (1·90–13·70)
Age <40 years	2·80 (1·05–7·60)
Steady sex-partner injected drugs	0·32 (0·11–0·92)
Men†	
Men who have had sex with men (past year)	8·80 (3·70–20·50)

Data missing for 20 individuals. *26 cases, 350 controls. †31 cases, 765 controls.

Table 5: **Risk factors for HIV seroconversion in multivariate analysis**

sex-partner who did not inject drugs, were combined with the category of having a steady sex-partner who injected drugs, because they had similar risk.

Table 5 shows multivariate analysis of risk factors for HIV-1 seroconversion, stratified by sex. The only significant variable for men was having sex with men in the past year. Significant risk factors for women were: traded sex for money in the past year, and being younger than 40 years. Women who reported having a steady sex-partner who injected drugs were less likely to seroconvert than those who did not.

Since our results indicate that gay men, and women who exchange sex for money, are at increased risk of seroconversion, we assessed the risk behaviours of the 14 gay male seroconverters and 17 female sex-worker seroconverters. Of the 14 gay male seroconverters, ten reported more than one male sex-partner in the past year, 13 reported not always using condoms, seven reported having shared a syringe in the past year, and one reported having shared a drug cooker in the past year. Of the 17 female sex-workers who seroconverted, five reported more than 30 male sex-partners in the past year, nine reported between five and 30 male sex-partners, 12 reported not always using condoms for vaginal sex, five reported sharing syringes, and three reported sharing drug cookers.

There was no significant interaction between time (March, 1986, to June, 1990; July, 1990, to June, 1994; and July, 1994, to January, 1998) and each variable in table 5. Furthermore, there was no significant interaction between observation window ($\leq$1 year *vs* >1 year) and each variable listed in table 5. Analyses that excluded the six seroconverters who knew they had seroconverted before their follow-up visits gave similar results to those in table 5. Nearly two-thirds of participants reported syringe exchange as their usual source of syringes (480/774 [62%] men and 245/370 [66%] women). Use of syringe-exchange programmes and HIV-1 seroconversion were not significantly linked in men (adjusted odds ratio 0·78 [95% CI 0·32–1·90]) or women (1·70 [0·51–5·90]).

Discussion

Our results show that the main risk factors for IDUs are sexual behaviours. The strongest predictor of HIV-1 seroconversion for men was having sex with men, whereas among women the strongest predictor was trading sex for money. These risk factors were reported by 53% of seroconverters. Strathdee and colleagues[19] also showed that sexual risks among IDUs were associated with seroconversion. These results suggest that HIV-1 prevention should be concentrated on sexual risk among IDUs.

The results of our study differ from those of other longitudinal studies of IDUs in that we did not find any strong evidence that injection risk factors were associated with seroconversion in multivariate analyses. Our results suggest that San Francisco's HIV-prevention programmes for IDUs have been successful at reducing injection-related risk behaviours. However, they do not suggest that injection risk can be ignored. Upper confidence limits on injection-related risk factors were still high, even though these estimates were not significant. Furthermore, injection risk could become more important if prevention efforts were relaxed. HIV-1 transmission might be reduced by incorporation of new sexual-risk-reduction strategies into existing programmes.

Even in the age of HIV and AIDS, IDUs have been slow to reduce their sexual risk.[9,20] Sexual risk interventions for IDUs based on research, have used psychological models to guide single-person,[21] peer-based small-group,[22] and community-level[23] programmes. Some of these interventions have had success among non-IDU populations,[24,25] but fewer have been successful for IDUs.[20,26] Furthermore, even when proven successful, research-driven sexual interventions have rarely been used by community-based organisations, because they can be impractical or expensive. Collaboration between organisations and researchers would improve the practicality of interventions.

Gay male IDUs are thought to be at high risk because of high HIV-1 prevalence among the people with whom they engage in risky behaviours.[27] We could not find any published assessments of sexual interventions for these individuals. Thus, we suggest that research and harm-prevention programmes should be aimed at gay male IDUs. Research on gay male IDUs might help us to apply the work done on sexual-risk reduction among gay men to these people.[25,28]

Our results confirm those of other studies[29,30] in that female sex-workers are at high risk of HIV-1. Female sex-workers can be infected with HIV-1 by having unprotected sex with a large number of partners, even if most of their partners are uninfected.[31] San Francisco has several HIV-prevention programmes for such workers, including community health outreach, HIV testing, support groups, and workshops. Strategies to enable female sex-workers to practise safe sex, including client education, might help reduce HIV risk.

In our study, young IDU women were more likely than older IDUs to seroconvert, which was also shown in a study in Baltimore,[19] USA. These results suggest that young, female IDUs need HIV-prevention programmes.[32] Female IDUs, who reported that they had a steady sex-partner who was an IDU, were less likely than other women to seroconvert—possibly because women in stable sexual relationships with other IDUs are less likely to engage in risky drug use or sex with other people.

Many researchers have studied the effectiveness of syringe-exchange programmes.[33–35] These programmes are designed to decrease injection-related risks, which were not strongly associated with HIV-1 seroconversion in our study. Hence, we were not surprised that there was no significant association between syringe-exchange use and HIV-1 seroconversion. We[36] applied multivariate models to the same dataset and found that among IDUs who shared syringes at baseline, those who used syringe-exchange programmes were more likely than those who did not to have stopped sharing syringes at follow-up. Those findings support others that indicate that syringe exchange is an effective HIV-1-prevention programme.[33–35,37,38] Paone and colleagues[39] suggested that sexual-risk interventions could be done at syringe-exchange programmes.

Our study has some limitations. First, the targeted sampling technique used to recruit respondents made it impossible to generalise our findings to all IDUs in San Francisco. Because drug use is illegal, no sampling technique can randomly select drug users. Further, we cannot derive true refusal rates, since IDUs who did not wish to participate did not come to our field sites, and therefore cannot be counted. An estimated 17 000 IDUs live in San Francisco,[11] and during the 12 years of our study we interviewed 6115. However, although a substantial proportion of IDUs in San Francisco participated, we cannot know whether our study has a participation bias. Furthermore, retention bias might affect our results. 35% of participants returned for a follow-up visit. Our study was not designed as a cohort study—ie, participants returned of their own accord. Individuals who returned differed slightly from those who did not in ethnic origin, age, homelessness, cocaine use, speedball use, sharing of syringes, drug

treatment, and number of years of injection behaviour.

Another limitation is the possibility of bias in self-reported data because of social desirability, poor recall, and intoxication. However, multicentre-survey research[40] has shown that self-report is very reliable among drug users not recruited in clinical settings. Because most of our cases did not know that they had seroconverted when they were interviewed, we do not believe that cases and controls differed in self-report validity. Finally, our matched case-control design prevented us from estimating HIV-incidence rates or examining time as a risk factor.

We recommend that various settings, including streets, syringe-exchange programmes, drug-treatment programmes, prisons, and hospitals are looked at as appropriate venues for sexual-risk prevention programmes for IDUs. Workers in existing programmes, in which they help IDUs to reduce their injection-related-risks, should continue their efforts and think about implementing sexual-risk prevention as well.

Contributors

Alex Kral, Jennifer Lorvick, and Ricky Bluthenthal devised the report. Alex Kral, Ricky Bluthenthal, Peter Bacchetti, and Brian Edlin designed the study. Jennifer Lorvick was responsible for data acquisition. Alex Kral did the main statistical analyses. Ricky Bluthenthal, Lauren Gee, Peter Bacchetti, and Brian Edlin contributed to analyses. Alex Kral wrote the manuscript. All investigators commented on and amended report drafts.

Acknowledgments

We thank the following people for their contributions: Kristen Clements, Donny Gann, Chris Kolb, Kelly Ray Knight, Jeffrey Moore, Michael Ray, Arthur Reingold, Donald Seeberg, David Vlahov, and John K Watters.

The study was funded by the National Institute on Drug Abuse (R01-DA12109), Universitywide AIDS Research Program of University of California, and San Francisco Department of Public Health.

References

1 Holmberg SD. The estimated prevalence and incidence of HIV in 96 large US metropolitan areas. *Am J Public Health* 1996; **86:** 6442–654.
2 van Ameijden EJ, van den Hoek JA, van Haastrecht HJ, Coutinho RA. The harm reduction approach and risk factors for human immunodeficiency virus (HIV) seroconversion in injecting drug users, Amsterdam. *Am J Epidemiol* 1992; **136:** 236–43.
3 Nicolosi A, Musicco M, Saracco A, Molinari S, Ziliani N, Lazzarin A. Incidence and risk factors of HIV infection: a prospective study of seronegative drug users from Milan and northern Italy, 1987–1989. *Epidemiology* 1990; **1:** 453–59.
4 Friedman SR, Jose B, Deren S, Des Jarlais DC, Neaigus A. Risk factors for human immunodeficiency virus seroconversion among out-of-treatment drug injectors in high and low seroprevalence cities. *Am J Epidemiol* 1995; **142:** 864–74.
5 Moss AR, Vranizan K, Gorter R, Bacchetti P, Watters J, Osmond D. HIV seroconversion in intravenous drug users in San Francisco, 1985–90. *AIDS* 1994; **8:** 223–31.
6 Solomon L, Astemborski J, Warren D, et al. Differences in risk factors for human immunodeficiency virus type 1 seroconversion among male and female intravenous drug users. *Am J Epidemiol* 1993; **137:** 892–98.
7 Rhodes T, Stimson GV, Crofts N, Ball A, Dehne K, Khodakevich L. Drug injecting, rapid HIV spread, and the 'risk environment': implications for assessment and response. *AIDS* 1999; **13** (suppl A): 259–69.
8 Kral AH, Bluthenthal RN, Booth RE, Watters JK. HIV seroprevalence among street-recruited injecting drug and crack cocaine users in 16 US municipalities. *Am J Public Health* 1998; **88:** 108–13.
9 Watters JK. Trends in risk behaviors and HIV seroprevalence in heterosexual injection drug users in San Francisco, 1986–1992. *J Acquir Immune Defic Syndr Hum Retrovirol* 1994; **7:** 1276–81.
10 Kral AH, Bluthenthal RN, Erringer EA, Lorvick J, Edlin BR. Risk factors among IDUs who give injections to or receive injections from other drug users. *Addiction* 1999; **94:** 675–83.
11 San Francisco Department of Public Health. HIV prevalence and incidence in San Francisco. San Francisco: HIV Seroepidemiology Unit, San Francisco Department of Public Health, 1997.
12 Fisher DG, Fenaughty AM, Trubatch B. Seroconversion issues among out-of-treatment injection drug users. *J Psychoactive Drugs* 1998; **30:** 299–305.
13 Kellogg T, McFarland W, Katz M. Recent increases in HIV seroconversion among repeat anonymous testers in San Francisco. *AIDS* 1999; **13:** 2303–04.
14 McFarland W, Kellog TA, Dilley J, Katz MH. Estimation of human immunodeficiency virus (HIV) seroincidence among repeat anonymous testers in San Francisco. *Am J Epidemiol* 1997; **146:** 662–64.
15 DesJarlais DC. Harm reduction: a framework for incorporating science into drug policy. *Am J Public Health* 1995; **85:** 10–12.
16 Bluthenthal RN, Kral AH, Erringer EA, Edlin BR. Use of an illegal syringe exchange and injection-related risk behaviors among street-recruited injection drug users in Oakland, California, 1992–1995. *J Acquir Immune Defic Syndr Hum Retrovirol* 1998; **18:** 505–11.
17 Watters JK, Biernacki P. Targeted sampling: options for the study of hidden populations. *Soc Problems* 1989; **36:** 416–30.
18 Centers for Disease Control and Prevention. Interpretive criteria used to report western blot results for HIV-1-antibody testing—United States. *MMWR Morb Mortal Wkly Rep* 1991; **40:** 692–95.
19 Strathdee SA, Galai N, Safaiean M, et al. Gender differences in risk factors for HIV seroconversion among injection drug users: a ten year perspective. *Arch Intern Med* (in press).
20 Rhodes T, Stimson GV, Quirk A. Sex, drugs, intervention, and research: from the individual to the social. *Subst Use Misuse* 1996; **31:** 375–407.
21 Calsyn DA, Saxon AJ, Wells EA, Greenberg DM. Longitudinal sexual behavior changes in injecting drug users. *AIDS* 1992; **6:** 1207–11.
22 Latkin CA. Outreach in natural settings: the use of peer leaders for HIV prevention among injecting drug users' networks. *Public Health Rep* 1998; **113** (suppl): 151–59.
23 The CDC AIDS Community Demonstration Projects Research Group. Community-level HIV intervention in 5 cities: final outcome data from the CDC AIDS community demonstration projects. *Am J Public Health* 1999; **89:** 336–45.
24 Downing M, Knight KR, Vernon KA, et al. This is my story: a descriptive analysis of a peer education HIV/STD risk reduction program for women living in housing developments. *AIDS Educ Prev* 1999; **11:** 43–61.
25 Kelly JA, Murphy DA, Sikkema KJ, et al. Randomised, controlled, community-level HIV-prevention intervention for sexual-risk behaviour among homosexual men in US cities. Community HIV Prevention Research Collaborative. *Lancet* 1997; **350:** 1500–05.
26 Calsyn DA, Saxon AJ, Freeman G, Whittaker S. Ineffectiveness of AIDS education and HIV antibody testing in reducing high-risk behaviors among injection drug users. *Am J Public Health* 1992; **82:** 573–75.
27 Centers for Disease Control and Prevention. HIV/AIDS among men who have sex with men and inject drugs—United States, 1985–1998. *MMWR Morb Mortal Wkly Rep* 2000; **49:** 465–70.
28 Kegeles SM, Hays RB, Coates TJ. The Mpowerment Project: a community HIV prevention intervention for young gay men. *Am J Public Health* 1996; **86:** 1129–36.
29 Edlin BR, Irwin KL, Faruque S, et al. Intersecting epidemics—crack cocaine use and HIV infection among inner-city young adults. *N Engl J Med* 1994; **331:** 1422–27.
30 Astemborski J, Vlahov D, Warren D, Solomon L, Nelson KE. The trading of sex for drugs or money and HIV seropositivity among female intravenous drug users. *Am J Public Health* 1994; **84:** 382–87.
31 Elifson KW, Boles J, Darrow WW, Sterk CE. HIV seroprevalence and risk factors among clients of female and male prostitutes. *J Acquir Immune Defic Syndr Hum Retrovirol* 1999; **20:** 195–200.
32 Kral AH, Lorvick J, Edlin BR. Sex- and drug-related risk among populations of younger and older injection drug users in adjacent neighborhoods in San Francisco. *J Acquir Immune Defic Syndr Hum Retrovirol* 2000; **24:** 162–67.
33 Normand J, Vlahov D, Moses LE. Preventing HIV transmission: the role of sterile needles and bleach. Washington, DC: National Academy Press, 1995.
34 National Institutes of Health. Interventions to prevent HIV risk behaviors. *NIH Consensus Statement* 1997; **15:** 1–41.
35 Lurie P, Reingold AL, Bowser B, et al. The public health impact of needle exchange programs in the United States and abroad. San Francisco: University of California, 1993.
36 Kral AH, Bluthenthal RN, Lorvick J, Bacchetti P, Gee L, Edlin BR. Effect of syringe exchange utilization on a cohort of syringe sharing IDUs in San Francisco, 1989–1998. 127th meeting of the American Public Health Association 1999, Chicago, IL.
37 Watters JK, Estilo MJ, Clark GL, Lorvick J. Syringe and needle exchange as HIV/AIDS prevention for injection drug users. *J Am Med Assoc* 1994; **271:** 115–20.
38 Bluthenthal RN, Kral AH, Gee L, Erringer EA, Edlin BR. The effect of syringe exchange use on high-risk injection drug users: a cohort study. *AIDS* 2000; **14:** 607–11.
39 Paone D, Caloir S, Shi Q, Des Jarlais DC. Sex, drugs, and syringe exchange in New York City: women's experience. *J Am Med Wom Assoc* 1995; **50:** 109–14.
40 Weatherby N, Needle R, Cesari H, et al. Validity of self-reported drug use among injection drug users recruited through street outreach. *Eval Prog Plan* 1994; **17:** 347–55.